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Epidemiology of heart failure in a community-based study of subjects aged ≥ 57 years: Incidence and long-term survival

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Abstract

Background: Survival data from hospital-based or clinical trial studies of patients with chronic heart failure (CHF) do not represent survival in community-based settings.

Aims: To determine the incidence of CHF and the associated long-term survival in a community-based sample aged ≥ 57 years and to assess the mortality risk associated with sex and age.

Methods: This study was part of the Groningen Longitudinal Aging Study.

Results: Annual incidence of CHF per 1000 ranged from 2.5 in middle aged adults (57–60 years) up to 22.4 in older females (≥ 80 years) and 28.2 in older males (≥ 80 years). The 1, 2, 5 and 7-year survival rates were 74%, 65%, 45%, 32% for patients with CHF, compared to 97%, 94%, 80% and 70% in a matched reference group without CHF. Higher age (≥ 76 years) was a risk factor for mortality (OR=2.1) and male sex was a risk factor in those aged ≤ 75 years (OR=1.9) but not for older patients.

Conclusion: Long-term survival rates for patients with CHF in the community were worse than the known survival rates from clinical trials. There is a need for studies describing the care of patients with CHF in the community, including the type of care, the provider, the quality of care and the outcome.

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Keywords: Heart failure; Survival; Incidence; Epidemiology; Elderly; Sex

1. Introduction

Chronic heart failure (CHF) is a common and growing health problem especially among the elderly. Despite advances in therapeutic interventions, CHF has a poor prognosis both in terms of morbidity and mortality. Estimates of mortality among CHF patients are available from various sources, including clinical trials, hospital-based studies and community-based samples. Data on long-term mortality are often lacking in clinical trials. An

exception is the COMET trial which reports a 5-year mortality rate of 35%–41% [1]. Hospital-based studies include patients who are selected during hospitalization for CHF or from hospital outpatient settings. Such hospital-based studies, report 5-year mortality rates of 48% [2] and 77% [3] compared to 45%–67% for community-based samples [4–6]. A recent large community-based study in the UK reported 3-year mortality rates of 67% in male and 60% in female patients with CHF [7]. Clearly, estimates of long-term mortality differ according to the source of the data. Moreover, data from the 1980s may not be representative of the current situation, since new therapies for CHF, such as angiotensin-converting-enzyme-inhibitors and beta-

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blockers have been introduced since then. Recent clinical trials on therapeutic interventions among CHF patients show that these advances in therapy increase survival [3,8–11]. Recent large clinical trials suggest that the annual mortality rate among patients with CHF is approximately 10% [1,12–14]. It is, however, questionable whether these trends in CHF survival seen in clinical trials are applicable to patients in the community [15–17].

Most patients with CHF are treated in the community, but the evidence base for their treatment is largely derived from clinical trials and observational studies of hospital-based patients. A number of variables distinguish patients with CHF who are recruited for clinical trials from those in hospital or community settings. Patients in clinical trials are more likely to be male, more likely to have their diagnosis corroborated by structured assessment and formalized criteria and less likely to have medical comorbidities that may contribute directly to mortality and complicate the management of CHF [18]. In addition, patients in the community are about a decade older than patients in clinical trials [19]. Estimates of mortality in hospital-based studies are also from selected populations, since they select patients from consecutive hospital admissions or hospital outpatient settings, who are more likely to be treated by cardiologists rather than solely relying on primary care physicians. These differences may limit the validity of comparisons between these three types of CHF patient.

The objective of this study was therefore to determine the incidence (in age and sex strata) and long-term survival of CHF in a community based sample of subjects aged ≥ 57 years; and to assess the mortality risk associated with sex and age. In addition, survival rates will be compared to sex–age matched subjects without CHF.

2. Methods

This study was part of the Groningen Longitudinal Aging Study (GLAS). In this community-based sample of subjects aged 57 years or older, incident cases of CHF were identified by general practitioners between 1993 and 1998 and survival data were collected up to 2001.

2.1. Groningen longitudinal aging study

A detailed description of data collection has been published elsewhere [20–23]. Briefly, the source population was late middle-aged and older adults, living independently or in old people's homes in the northern part of the Netherlands. The study population comprised 8723 subjects aged 57 years or older on January 1, 1993, who were registered as patients with the 27 general practitioners participating in the Morbidity Registration Network Groningen. In the Netherlands, nearly 100% of non-institutionalized older adults are registered with a general practitioner's practice. A total of 1937 subjects refused to

participate (22%). Of the remaining 6786, 1277 declined to participate when contacted by the research team, and 152 had died or left the practice by the time contact was initiated. Another 78 subjects were excluded because of severe cognitive impairment at baseline (Mini-Mental State Examination Score of 16 or lower). Useful baseline data were available for 5279 subjects (62%; 5279/(8723–152)) (see Appendix). The GLAS baseline assessment was carried out in 1993 and consisted of an interview and a questionnaire sent by mail. Non-response was associated with age (34% non-response for subjects aged 57 to 69, 42% for subjects aged 70 to 84, and 67% for subjects 85 years or older) and with sex (37% non-response for men, 41% for women). The characteristics of the GLAS baseline sample were assessed by comparisons on four clusters of physician-registered morbidity. There was a higher proportion of patients with malignant neoplasm among non-responders, but no significant differences were found for ischemic heart disease and CHF, chronic respiratory diseases and chronic diseases of the locomotor apparatus [20,21]. The GLAS baseline study and its follow-up studies were approved by the local medical ethics committee and all participants gave written consent to participate in the study.

2.2. New patients with CHF

New patients with CHF were recruited from the 5279 GLAS baseline participants through the 27 general practitioners participating in the Morbidity Registration Network Groningen. From the baseline wave in 1993 until January 1, 1998, these physicians passed on the names of all patients with a new diagnosis of CHF according to the criteria of the International Classification of Primary Care (ICPC) [24]. Subjects who were diagnosed with CHF before 1993 were excluded from the cohort. CHF was diagnosed if three of the following five symptoms were present: (a) dependant oedema, (b) raised jugular venous pressure or hepatomegaly in the absence of liver disease, (c) signs of pulmonary congestion or pleural effusion, (d) enlarged heart or (e) dyspnoea in the absence of pulmonary disease (code K77 of the ICPC). During the enrolment period (1993–1998), 293 patients with a first diagnosis of CHF after baseline were recruited. The mean time interval between the baseline interview and the diagnosis of CHF was 28 months and ranged from 15 days to 5 years.

2.3. Subjects without CHF

All 4986 GLAS participants who did not have a new diagnosis of CHF (between 1993–1998) were included in the study to calculate the incidence rates of CHF for each sex–age stratum. In addition, reference subjects (matched according to sex and age ± 1 years) were selected from these 4986 subjects without CHF. According to these rules, two matched reference subjects were successfully identified for each of the 293 patients. These reference subjects did not

develop CHF between 1993 and 1998, but they may have had other chronic diseases. The purpose of this matched reference group was to illustrate the mortality risk in a sample without CHF with a comparable sex and age distribution.

2.4. Mortality

Survival status was checked for all patients and reference subjects at approximately 8 years after the baseline assessment in 1993 (i.e. June 1st, 2001). Data on all-cause mortality were collected using municipal registrations.

2.5. Baseline characteristics

Sex, age, educational level, marital status, and comorbidity were assessed at the baseline interview in 1993. Prevalence of (other) chronic diseases was assessed using a checklist, comprising 19 chronic medical conditions: asthma or chronic bronchitis, pulmonary emphysema, heart condition, hypertension, (consequences of) stroke, leg ulcer, stomach ulcer, liver disorder or gallstones, kidney disease, prostate problem, diabetes mellitus, thyroid gland disorder, back problems for at least 3 months or slipped disc, joint conditions or arthritis, migraine or chronic headache, serious dermatological disorders, cancer, multiple sclerosis, Parkinson's disease or epilepsy. Participants were asked whether they suffered from one or more of these conditions in the 12 months prior to the interview. In order to reduce report-bias, only those conditions that required a GP or specialist consultation and/or prescription of medicine were counted. This procedure was similar to procedures used by the Netherlands Central Office of Statistics in periodic health surveys [25].

2.6. Analyses

Incidence rates for CHF according to sex and age strata were calculated by dividing the total number of incident CHF cases in each stratum by the total number at risk (i.e. incidence in 5 years (1993–1998)). Annual incidence rates were calculated by dividing these 5-year incidence rates by 5.

Baseline characteristics of CHF patients ($n=293$) and GLAS subjects who did not develop CHF ($n=4986$) were compared using *t*-test and Chi-square tests. A *P* value of <0.05 was considered significant. Kaplan–Meier survival tables and curves were calculated for CHF patients and sex–age matched reference subjects. Survival rates were presented for patients at 1 month, 6 months, 1 year, 2, 3, 4, 5, 6 and 7 years after diagnosis. For reference subjects the survival rates at the same intervals since the baseline assessment in 1993 were presented. Kaplan–Meier survival tables were used to estimate the survival rates and 95% Confidence Intervals (95% C.I.) at several intervals. Survival curves for patients and reference subjects were presented according to sex and age (subjects aged ≤ 75

years versus subjects aged ≥ 76 years). A cut off score of 75 years was used to create two groups of equal size.

In addition, COX-proportional-hazard analyses were performed to calculate the hazard rates associated with CHF, sex and age. Among CHF patients, hazard rates (Odds Ratios) for mortality were presented for males versus females and for subjects aged ≤ 75 years versus subjects aged ≥ 76 years. Analyses were performed using SPSS for Windows version 12.

3. Results

3.1. Incidence of CHF in GLAS study

From the 5279 subjects who participated in the GLAS baseline assessment in 1993, a total of 293 subjects developed CHF in a 5 year period (1993 and 1998). Annual incidence rates of CHF among the GLAS subjects, according to sex and age are presented in Fig. 1. CHF incidence increased with age, and was somewhat higher among males than females.

3.2. Characteristics of patients developing CHF and subjects without CHF

Characteristics of patients developing CHF and all other GLAS subjects are presented in Table 1. Compared to GLAS subjects who did not develop CHF between 1993 and 1998, the 293 CHF patients were significantly older (mean age at baseline 75.5 years), were less well educated and more often lived without a partner (43%). In addition, CHF patients had more chronic conditions at baseline (mean=1.7) compared to GLAS subjects who did not develop CHF, and were significantly more likely to suffer from hypertension (29%), cardiac disease with no further detail (40%), diabetes (14%), asthma or chronic bronchitis (18%) and pulmonary emphysema (9%). The percentage of patients suffering the consequences of stroke and other chronic conditions (data not shown) and the percentage of

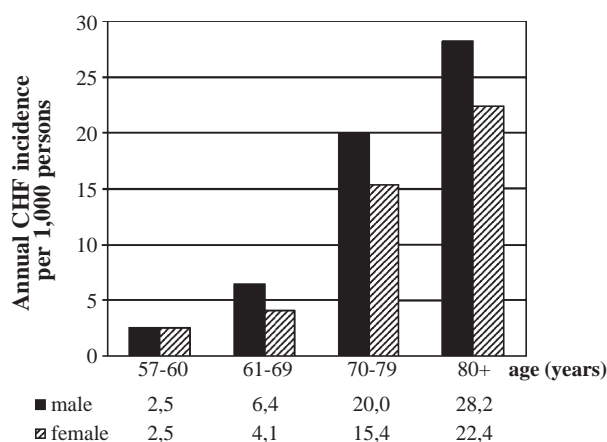


Fig. 1. Incidence rates of CHF among GLAS subjects by sex and age.

Table 1
Baseline characteristics of GLAS subjects who developed CHF and those who did not between 1993–1998

Characteristics at baseline in 1993	CHF patients (n=293)	Subjects who did not develop CHF between 1993–1998 (n=4986)	P value
Age in years			
Mean (SD)	75.5 (7.4)	69.2 (7.9)	<0.001
Range	58–96	57–99	
Sex			
% Females	52	56	0.157
Marital status			
% Without partner	43	32	<0.001
Educational level			
% Low	43	35	0.017
% Medium	49	54	
% High	8	11	
No. of chronic diseases			
Mean (SD)	1.7 (1.4)	1.1 (1.2)	<0.001
Range	0–7	0–10	
% Subjects with no. of chronic diseases			
None	20	36	<0.001
1	33	33	
2	22	18	
3 or more	25	13	
% Hypertension	29	22	0.009
% Cardiac disease with no further detail	40	19	<0.001
% (Consequences of) stroke	4	2	0.128
% Diabetes Mellitus	14	7	<0.001
% Asthma or chronic bronchitis	18	9	<0.001
% Pulmonary emphysema	9	3	<0.001

females did not differ significantly between CHF patients and the GLAS subjects who did not develop CHF between 1993 and 1998.

3.3. Survival rates among patients and sex–age matched reference subjects

The survival rates among CHF patients and sex–age matched reference subjects are presented in Table 2. For CHF cases, survival since diagnosis is presented. Patients

were diagnosed between 1993 and 1998, and survival status was evaluated in 2001. Consequently, a minimum follow-up since diagnosis of 3 years was available for all patients, while a 7-year follow-up was available for 66% of patients. For the reference subjects, the survival rates are presented since the baseline assessment, which was performed in 1993 for all subjects. Therefore, follow-up is complete up to 7 years for all reference subjects. Among CHF patients, 74% survived the first year, in other words 26% of patients died within the first year following diagnosis. Subsequent annual mortality rates among survivors were 12%, 14%, 9%, 11%, 14% and 18%, respectively, in the second to seventh years. At 7-year follow-up, survival among CHF patients was 32%, compared to 70% among sex–age matched reference subjects. Survival among patients with CHF was markedly decreased compared to the sex–age matched reference group without CHF. Compared to sex–age matched reference subjects, CHF was associated with a 3.7 fold increased mortality risk (Cox regression analyses: Odds Ratio=3.7, 95% C.I.: 2.97–4.56).

3.4. Mortality risks associated with sex and age

The Kaplan–Meier survival curves for patients and sex–age matched reference subjects are presented in Fig. 2A and B. Results are presented for patients and matched reference subjects aged ≤ 75 years and those aged 76 years or older separately. Fig. 2A shows that among those aged 75 years or less, both male patients and male reference subjects had worse survival compared to their female counterparts. Female patients aged ≤ 75 years (line C) had significantly better survival compared to male patients aged ≤ 75 years (line D). Fig. 2B shows that in the older age strata (≥ 76 years), male reference subjects had worse survival than female reference subjects, but no significant difference was observed between male and female CHF patients among these older patients. The mean survival times in these strata are presented below Fig. 2A and B and ranged from 71 months in female CHF patients aged ≤ 75 years to as little as 40 months in male CHF patients aged ≥ 76 years.

Cox regression analyses were performed to quantify the mortality risks associated with sex and age. Table 3 shows that male sex was associated with a 1.9 (95% C.I.: 1.16–3.11)

Table 2
Survival rates among CHF patients and sex–age matched reference subjects

	Survival rates at time intervals in percent (95% Confidence Interval)*								
	1 month	6 months	1-year	2-year	3-year	4-year	5-year	6-year	7-year
CHF patients (n=293)	90(87–93)	83(78–87)	74(69–79)	65(59–70)	56(51–62)	51(45–56)	45(39–51)	39(33–45)	32(25–39)
Reference subjects (n=586)	100-	99(98–100)	97(96–98)	94(92–96)	90(88–93)	86(83–89)	80(77–83)	74(70–78)	70(66–74)

* For CHF patients the interval represents the time since diagnosis. Patients were diagnosed between 1993 and 1998, and survival status was evaluated in 2001. Therefore, follow-up since diagnosis is complete up to 3 years; and 4-, 5-, 6- and 7-year follow-up is available for 96%, 84%, 72%, and 66% of patients, respectively.

For reference subjects the time intervals are since the baseline assessment, which was performed in 1993 for all subjects. Therefore, follow-up is complete up to 7 years for all reference subjects.

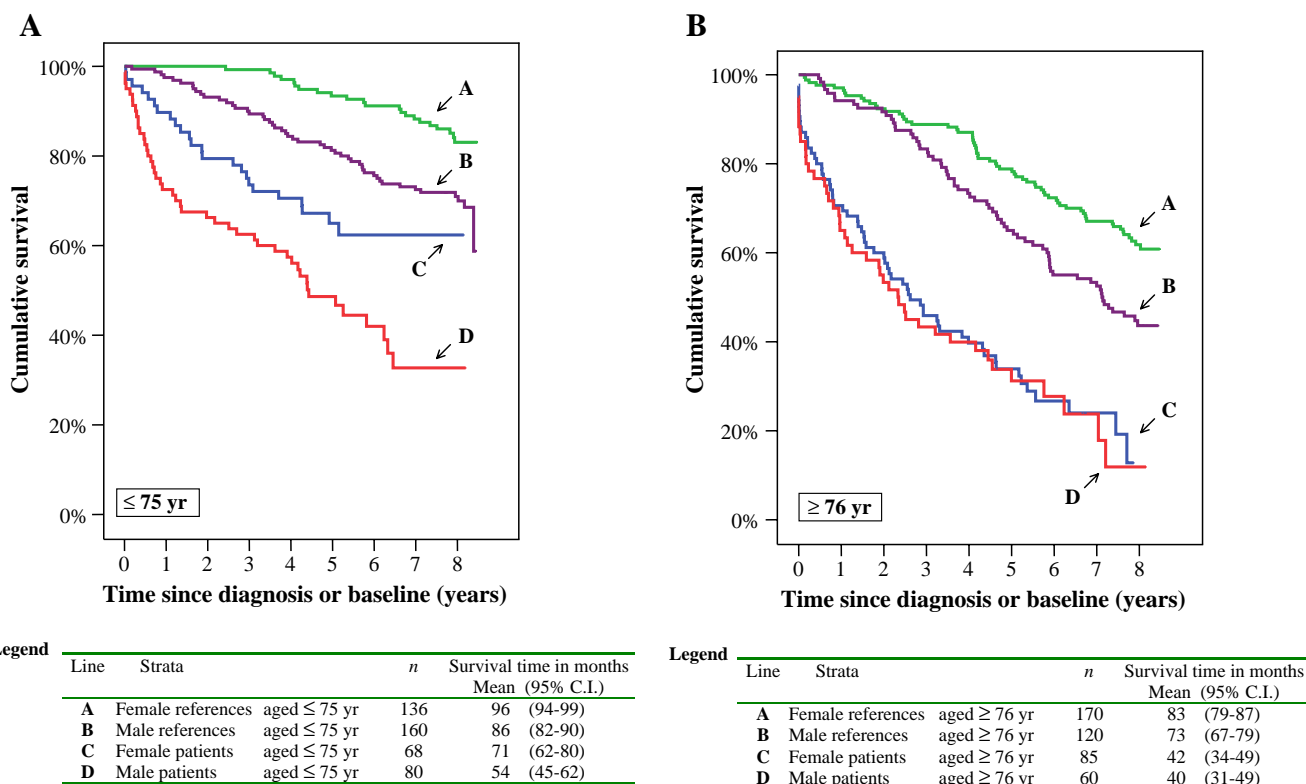


Fig. 2. Kaplan Meier survival curves for CHF patients since diagnosis and for sex–age matched reference subjects since baseline in those aged ≤ 75 years (A) and those aged ≥ 76 years (B).

increased risk for mortality compared to female patients aged ≤ 75 years, while male sex was not significantly related to an increased mortality risk among older patients. Patients with higher age (≥ 76 years) had a significant increased mortality risk compared to younger subjects, both among males (OR=2.8) and females (OR=1.6).

4. Discussion

This study reports the incidence and long-term survival rates for patients with chronic heart failure (CHF) in a community-based sample. The incidence of CHF clearly increases with age and is somewhat higher among males, which is in line with results from other epidemiological studies [26,27]. Long-term survival rates among CHF

patients were low. From a comparison with GLAS subjects who did not develop CHF between 1993–1998, it became clear that the average CHF patient is characterized by older age and having other chronic conditions, typically hypertension, diabetes mellitus or lung diseases. Clearly these characteristics contribute to the high mortality rates found in this study. Mortality rates which are derived from clinical trials suggest that the annual mortality rate among CHF patients is about 10% [1,12–14], however our study shows that mortality among CHF patients in the community is much higher, especially in the first year after diagnosis.

A number of factors are likely to contribute to the higher mortality rates observed in our community-based sample compared to mortality rates in clinical trials. The overall CHF population is older and has a higher comorbidity rate than populations in clinical trials [19]. Studies of CHF in the community generally describe prognosis from the onset of CHF. It is clear that many patients who develop CHF succumb rapidly to their condition and die within 1 to 6 months. The prognosis of patients with CHF who survive beyond these first few months in the community, is possibly more similar to that in clinical trials. However, if we focus on patients who survive the first 6 months (i.e. 83% of the original sample of patients), annual mortality rates among survivors still exceed 10%. Furthermore, the effectiveness of medical management is probably lower in a community based population than in patients managed by clinical trial investigators. Beyond potential differences in drug efficacy,

Table 3

Cox regression models for mortality among CHF patients showing Odds Ratios for sex and age

Characteristics of CHF patients (n=293)		Mortality Risk OR (95% C.I.) ^a	P value
Sex [0=female, 1= male]	All ages	1.4 (1.01–1.84)	0.041
	Age ≤ 75 years	1.9 (1.16–3.11)	0.011
	Age ≥ 76 years	1.1 (0.76–1.61)	0.551
Age [0= age ≤ 75 years, 1= age ≥ 76 years]	All sexes	2.1 (1.51–2.78)	<0.001
	Females	1.6 (1.06–2.42)	0.027
	Males	2.8 (1.73–4.46)	<0.001

^a OR=Odds ratio, C.I.=Confidence interval of odds ratio.

proven treatments are generally underused in the community [28]. To date ‘typical’ CHF patients have largely been excluded from clinical trials. This needs to change if the prognosis of CHF patients in the general population is to be improved [19].

Advances in therapeutic interventions for CHF have been shown to increase survival in hospital-based studies [3,8,9]. Evidence that the prognosis of CHF in the general population has improved over the past 50 years was found in the Framingham Heart Study and in other surveys [5,29]. In contrast, prognosis did not improve between 1981 and 1991 in the Rochester Epidemiology Project [6]. The continued gap between outcome advances observed in clinical trials versus the general community is disappointing. The fact that in both primary and secondary care the therapeutic management of CHF does not reflect current scientific evidence and is still far from optimal may contribute to the lower survival rates for CHF in the community [28].

A limitation of our study is that for case finding, this study depended on the diagnosis and clinical judgments of general practitioners, without confirming the diagnosis. Therefore, milder, unconfirmed cases of CHF are also included. On the other hand, milder cases may have been underrepresented in our study, since subjects with minor symptoms may wait before contacting their general practitioner. However, the incidence rates for CHF in this community-based cohort are comparable with rates found in the Framingham Heart Study [26]. Moreover, we were interested in survival of patients with (suspected) CHF according to the general practitioner. Most subjects with CHF remain in the care of primary physicians and therefore studying the outcome of patients identified by general practitioners as having CHF is important. The advantages of our study relate to the fact that it is a population-based study and included elderly participants. In the Netherlands, nearly 100% of non-institutionalized adults are registered with a general practitioner’s practice and the general practitioner must be contacted before obtaining specialized medical care. Consequently, all morbidity is registered by general practitioners, which makes our sample more representative of incident patients with CHF. In addition, we were able to collect information on vital status (including date of death) of all participants using municipal registrations.

The survival rates found in this community-based cohort of middle aged and older patients corresponds to rates found in large American studies, such as the Framingham Heart Study (1990–1999 cohort) [5] and the Rochester Epidemiological Project (1991 cohort) [6]. The slight differences between reported survival rates can be traced to CHF definition or study design. A population-based study in the UK reports a lower 1-year survival rate (62%) compared to the 74% in our study, which can be explained by the fact that diagnosis was confirmed by identifying an underlying cardiac dysfunction in the UK study, while in our cohort diagnosis was based on criteria in the general practice setting [30]. Such differences in survival rates between

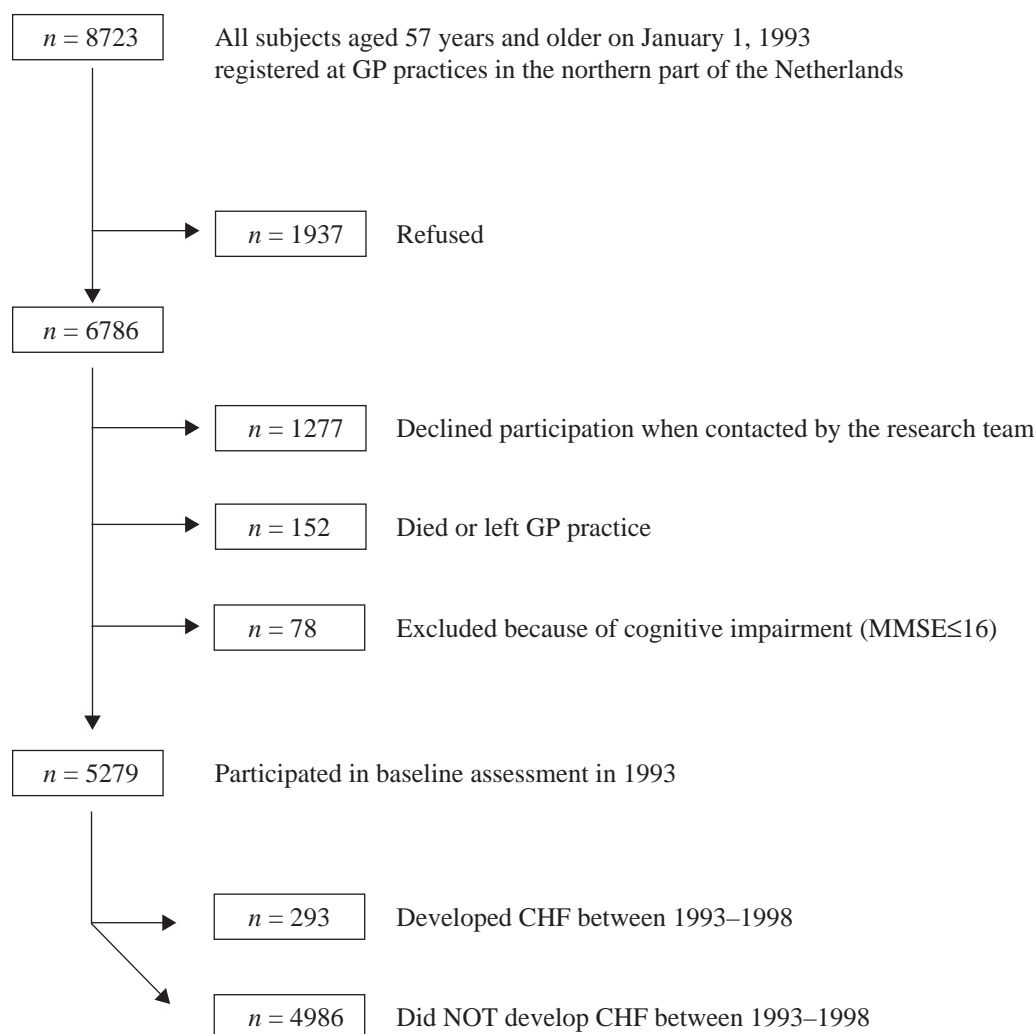
patients with definite versus possible CHF were recently reported in a general practice population [7]. The 5-year survival rate in our study is somewhat lower than in The Rotterdam Study (45% versus 59%), which may be related to the fact that we studied incident cases, while The Rotterdam study included prevalent cases [4].

Increasing age is a known risk factor for mortality both in the community and in patients with CHF [31,32]. Sex related differences in mortality have been reported, but results are contradictory. Higher mortality rates are reported for male compared to female patients with CHF [4,5,7,32]. Others have found no sex related effect [6,30,33] or report complex interactions between age and sex [3]. Our results show that male sex was related to increased mortality among patients aged ≤ 75 years only, while sex was not a significant risk factor among older patients (≥ 76 years). A recent community-based study in the UK also reported better survival among younger female patients, but not among older CHF patients [7]. The better survival among female patients (aged ≤ 75 years) is in contrast with reports of worse quality of life and more comorbidities in female compared to male CHF patients [34]. Sex related differences in aetiology and increased diastolic heart failure among females are suggested as explanations for this difference in mortality [35].

In conclusion, mortality rates for CHF are high, especially in the first year, but continue to be high in the long-term. Mortality is even higher among older patients, and among patients aged ≤ 75 year mortality is higher among males compared to females. Overall, long-term survival rates among patients with CHF from a community-based setting are even worse than the known survival rates from clinical trials. There is a need for studies that describe the care of patients with CHF in the community, including the type of care, the provider, the quality of care and the outcome.

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Appendix A. Flow chart of source population in the Groningen Longitudinal Aging Study (GLAS)**References**

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